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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,228	07/03/2003	Arthur M. Krieg	C1037.70045US00	4680

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,228	KRIEG, ARTHUR M.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-12,14,16-20,22,27-32 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 4 sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/27/04; 4/29/04*. 3 sheets total

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-20,22,27-32,43,45-57,63-65,70-73,76-80,83,84,88,89,94,95 and 97.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-7,13,15,45-57,63-65,70-73,76-80,83,84,88,89,94,95 and 97.

DETAILED ACTION

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. There is no claim 16. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 17-99 been renumbered 16-98. Applicant should correct the dependencies of the pending claims in response to this Office Action.

2. Applicant's amendment filed December 27, 2004 is acknowledged and has been entered. Claims 21, 23-26, 33-42, 44, 58-62, 66-69, 74, 75, 81, 82, 85-87, 90-93, 96 and 98 have been canceled. Claims 12, 45 and 97 have been amended. Claims 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95 and 97are now pending in the present application.

3. Applicant's election with traverse of Group I, claims 1-4, 8-12, 14, 16-20, 22, 27-32 and 43, elected species are cancer (specific antigen) and anti-cancer agent (specific therapeutic agent), in the reply filed on December 27, 2004 is acknowledged. The traversal is on the grounds that the Examiner has not met her burden under MPEP 806.05(h) as she has not provided examples of an alternative viable use for the composition of claim 1 or an alternative viable product to be used in the method claims with regard to Groups I and III. Applicant points out that the methods claims now recite the same product as set forth in claim 1. Applicant asserts that there is no basis for at least the position that the process of

using can be practiced with another materially different product. This is not found persuasive because any one of the numerous cancer vaccines set forth in Tables 2-4 of the specification can be used in the method of stimulating an immune response and/or treating cancer. Further, the product can be used in other treatment methods as set forth in Applicant's claims as well as for those methods of treatments of allergy, asthma, fungal infections, bacterial infections, and/or viral infections in a subject. With regard to Applicant's argument that there is no serious burden on the Examiner to consider Groups I and II together under MPEP 808.02. The two Groups have acquired a separate status in the art as a separate subject for inventive effect and require independent searches (see Restriction Requirement). The search for each of the above inventions is not co-extensive particularly with regard to the literature search. A reference, which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other groups. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist. Further, the two products are distinct because they are structurally different, they have different modes of operation and different functions when administered to a subject or used in *in vitro* methods.

Applicant's request for rejoinder once claims of Group I are found allowable, provided Group III claims depend from or otherwise include all limitations of allowable Group I claims is acknowledged. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the

product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments, submitted after final rejection, are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 5-7, 13, 15, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95 and 97 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and/or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 27, 2004.

5. Claims 1-4, 8-12, 14, 16-20, 22, 27-32 and 43 are being examined in this pending application.

6. The use of trademarks, see p. 88 and 95 for example, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

7. The disclosure is objected to because of the following informalities: incorrect table number for the table on page 89, this is not Table 1. Table 1 is on

pages 59-60. The reference citation on page 91 is incomplete. Appropriate correction is required.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-4, 8-11, 16-20, 29-32 and 43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-46, 52-56 and 58-60 of copending Application No. 10/816,220. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim a composition

comprising a immunostimulatory nucleic acid molecule, Applicant's SEQ ID NO: 1 is SEQ ID NO: 152 set forth in claim 56 of Application 10/816,220. Both applications set forth claims directed to the composition also comprising an antigen, which can be a cancer antigen as well as additional adjuvants and modes of administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-4, 8-11, 16-20, 29-32 and 43 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a composition comprising (or consisting of) SEQ ID NO: 1. The composition also comprises cancer antigen, adjuvants as well as anti-cancer agents. Based on the components of the composition it would appear that the intended use of the claimed composition is for *in vivo* use in a method to treat cancer in a subject. However, none of the examples set forth in the specification disclose the use of the claimed composition, that being a SEQ ID NO: 1 and a cancer antigen with any of the other possible components (cytokines, adjuvants, mucosal adjuvants and anti-cancer agents, etc) for treatment of a cancer in a subject.

The specification discloses the use of SEQ ID NO: 1 (ODN 10106) in *in vitro* assays that indicate that the nucleic acid can activate TLR9, human B cells and B cell proliferation, all *in vitro*. Th1 dominated immune responses were

observed and IFN-alpha secretion. The only *in vivo* evidence provided in the specification is found on page 95, where mice were immunized with ODN 10106 and HBsAg, an immune response was achieved. There is no evidence of *in vivo* use of the claimed composition comprising SEQ ID NO: 1, cancer antigen, with any of the other additional components. The specification does not predict or teach any positive therapeutic benefit (i.e. treating or preventing cancer or immune response) correlated with the administration of the claimed composition in a rodent or non-rodent subject.

The state of the art with regard to cancer is unpredictable. Tumor cells *in vivo* simply do not display their unique antigens in ways that are easily recognized by cytotoxic T lymphocytes (Ezzell; see also Forni et al). Tumors are classified as immunogenic or non-immunogenic, solid or hematological in nature. Effective cancer strategies should be designed to deal effectively with the nature of each of these classifications. Further, it has been an art-recognized experience that for any novel therapy, the transition from the laboratory to the clinic (animal experiments to bedside) is a quantum leap (Chatterjee et al.). Results obtained under controlled conditions and in inbred animals often differ from the clinical response obtained in patients. This applies in particular to strategies based on immune responses. McCluskie et al teaches that T-rich immunostimulatory nucleic acids do not induce an immune response. *In vitro* animal model studies have not correlated well with *in vivo* clinical trial results in patients. Since the therapeutic indices of immunotherapeutic regimens can be species- and model-dependent, it is not clear that reliance in the *in vitro* stimulation of immune cells with the claimed immunostimulatory nucleic acid and the *in vivo* mouse and non-human primate experimental models with CpG containing ODNs accurately reflects the relative

efficacy of the claimed therapeutic strategy based upon *in vitro* stimulation as disclosed in the specification.

There is insufficient evidence that would lead a person of skill in the art to predict that the claimed composition would have the ability to treat or prevent cancer or to induce an immune response in a subject. The specification provides insufficient guidance to practice the claimed invention. In view of the lack of the predictability of the art to which the invention pertains and the lack of established clinical protocols for effective adjuvant therapies, undue experimentation would be required to practice the claimed invention with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed invention.

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
March 20, 2005